Sudden Death Six Weeks After a Myocardial Infarct

FORRESTER LEE, M.D.,[a] STUART D. FLYNN, M.D.,[b]
AND ANA M. SALAZAR, M.D.[c]

[a]*Department of Internal Medicine,* [b]*Department of Pathology,* [c]*Department of
Diagnostic Radiology, Yale University School of Medicine, New Haven, Connecticut*

A 56-year-old man died suddenly at Yale–New Haven Hospital six weeks after experiencing a myocardial infarct and subsequent left ventricle aneurysm formation. Clinical course, treatment, radiologic data, and pathologic findings are examined. Differential diagnosis for this patient's sudden demise include cardiac rupture with cardiac tamponade, extension of the myocardial infarct, and massive pulmonary embolus, among others.

CLINICAL PATHOLOGICAL CONFERENCE

A 56-year-old man died suddenly at Yale–New Haven Hospital six weeks after experiencing a myocardial infarct and subsequent left ventricle aneurysm formation.

History

A 56-year-old male executive was transferred from another hospital because of recurrent cardiac arrhythmias. One year ago he developed substernal chest pain typical of angina pectoris. A well-documented acute anterolateral myocardial infarction precipitated his admission to another hospital one month ago. He suffered several prolonged episodes of ventricular tachycardia/fibrillation, which were unresponsive to lidocaine, associated with grand mal seizures, and treated by cardioversion. He subsequently developed right bundle branch block accompanied by left anterior hemiblock. During an attempt to insert a pacemaker, he had another grand mal seizure associated with ventricular tachycardia. In addition, he developed congestive heart failure which initially responded to digoxin and diuretics, staphylococcal sepsis which resulted from an infected line and was successfully treated with oxacillin, respiratory failure which required transient ventilatory assistance, and a low-grade fever which was attributed to Pronestyl.®

Episodes of ventricular tachycardia/fibrillation were eventually prevented by tocainide. Ten days before transfer, the patient was treated with heparin followed by Coumadin because of deep venous thrombosis of the left calf. Cardiac ultrasound demonstrated a left ventricular aneurysm. Congestive heart failure became increasingly difficult to manage, and attempts to reduce afterload with captopril, nitrates, or nifedipine were frustrated by hypotension. Two days before transfer, he again developed recurrent episodes of ventricular tachyarrhythmia which could be controlled only by continuous infusion of bretylium.

Aside from 120 pack-years of cigarette smoking, there were no risk factors for coronary artery disease, and the remainder of the history was not contributory.

At the time of transfer, the patient was alert but appeared ill. Except for jugular venous distention, rales at both lung bases, and a third heart sound, no specific physical findings were elicited by three examiners.

Chext X-ray showed only increased pulmonary congestion. The cardiac silhouette was at the upper limits of normal. Electrocardiogram showed an extensive infarction with Q waves in leads V_2 through V_6. Right bundle branch block (RBBB) and left anterior hemiblock (LAHB) were also confirmed. Except for a hematocrit of 30 percent, complete blood count and electrolytes were normal except for Na, 127; BUN, 35; creatinine, 1.6, and a prothrombin time of 16.0/12.2.

Coumadin was stopped, and intravenous heparin was begun. Hyponatremia was readily corrected by volume restriction. Electrophysiologic studies and aneurysmectomy were considered, but 12 hours after admission the patient developed prolonged ventricular tachycardia, persistent hypotension, and respiratory failure. He required cardioversion, an intra-aortic balloon, tracheal intubation, a pacemaker, and hemodynamic monitoring with a Swan-Ganz catheter. The following morning he had an emergency cardiac catheterization, which showed a large left ventricular aneurysm and 90 percent stenosis of the left anterior descending artery. Because of episodes of ventricular tachycardia, Amiodarone was instituted, and the patient's condition became stable. On the fifth hospital day, he was extubated and the intra-aortic balloon was removed. Because he needed frequent repeated blood transfusions to maintain his hematocrit above 30 percent, heparin was discontinued on the fifth hospital day. Despite continuing congestive failure with an ejection fraction of only 9 percent, the patient was able to walk to a limited extent and had no further episodes of tachyarrhythmia while receiving Amiodarone. On the tenth hospital day, however, he suddenly collapsed to the floor. Despite resuscitation for cardiopulmonary arrest, the patient expired.

Clinical Discussion

DR. FORRESTER LEE *(Assistant Professor of Medicine):* In summary, a 56-year-old man who sustained an anterior wall myocardial infarction (AMI) complicated by ventricular arrhythmias, aneurysm formation, and congestive heart failure, died suddenly in the hospital after six weeks. I will first comment on his clinical course and then discuss the differential diagnosis.

The patient was admitted to another hospital with an acute anterior infarction and recurrent ventricular arrhythmias. Since we do not have many details from his early hospital course, let me skip ahead in the protocol and note that a left ventricular aneurysm was documented during a later echocardiographic examination. This finding helps us to reconstruct some of the pathogenic processes which developed early during his infarction and probably formed the basis for his subsequent cardiac complications.

Ventricular aneurysm formation following acute myocardial infarction has a well-characterized temporal development. From serial echocardiographic and radionuclide studies, we know that, during the first 48 hours following AMI, some ventricles undergo a process termed "infarct expansion." The left ventricle appears regionally dilated with cavity deformation and myocardial thinning. These anatomic features are typical of chronic ventricular aneurysms which all appear to begin as regional infarct

expansion. Of particular relevance in this case, infarct expansion and cardiac rupture have been very closely linked. Schuster and Bulkley found that 23 of 24 autopsy heart specimens with cardiac rupture had anatomic and pathological features of infarct expansion [1].

Cardiac rupture is the second most common in-hospital cause of hemodynamic-related deaths following acute infarction. It is, nonetheless, an uncommon event with an incidence of less than 1 percent among transmural infarctions. On the other hand, infarct expansion has been shown to develop in as many as 35 percent of acute myocardial infarction (MI) patients. Though infrequently leading to cardiac rupture, infarct expansion and aneurysm formation are clearly linked to a high incidence of other cardiac-related complications, including arrhythmias, congestive heart failure, and sudden death [2], all of which occurred in this patient. Thus infarct expansion represents a cardinal event in this patient's course and must be considered in formulating a differential diagnosis.

During his early hospitalization, there were other clinical events which might have been a factor in his later death. A temporary transvenous pacemaker was placed for bifascicular heart block. Among the several complications that can arise from temporary pacemaker insertions are venous thrombosis and pacemaker rupture of the right ventricle. This patient in fact developed a clinically documented left calf thrombosis and was started on anticoagulant therapy. I would suspect that the temporary pacemaker was a factor in initiating the venous thrombotic process. When looked at by sensitive techniques, venous thrombosis can be documented following 40 percent of transvenous pacemaker insertions. Although these are usually clinically silent, there are well-documented cases of fatal thromboembolic complications related to transvenous pacemakers [3].

In spite of the early complications of arrhythmias, severe congestive heart failure, sepsis, and venous thrombosis, the patient was stabilized sufficiently to permit transfer to Yale–New Haven Hospital after three weeks. Perhaps now it would be timely to review his chest X-ray.

Radiologic Studies

DR. ANA M. SALAZAR *(Resident in Radiology, Yale–New Haven Hospital):* The admission chest radiography is a portable film (Fig. 1). The heart is enlarged and has a prominent left ventricular configuration. There is engorgement of the central vasculature and haziness of the peripheral vascular markings, indicating interstitial pulmonary edema. In this single projection, there is no definite evidence of a discrete left ventricular aneurysm since the cardiac contour is smooth. A central venous catheter is noted. There is no pneumothorax.

A follow-up film taken the next day demonstrates persistent congestive heart failure (Fig. 2). The patient has been intubated and an intra-aortic balloon pump is visible in good position. A Swan-Ganz catheter and a transvenous pacemaker have been inserted via a femoral approach.

DR. LEE: Thus the chest X-ray confirms the congestive heart failure and cardiomegaly that were apparent clinically. A temporary pacemaker inserted from a femoral location is present on the second X-ray. Therefore, we must keep open the possibility of a pacemaker-related complication. Soon after arrival, the patient again developed intractable arrhythmias with hemodynamic deterioration and required cardiopulmonary resuscitation. An intra-aortic balloon pump (IABP) was inserted. Although this
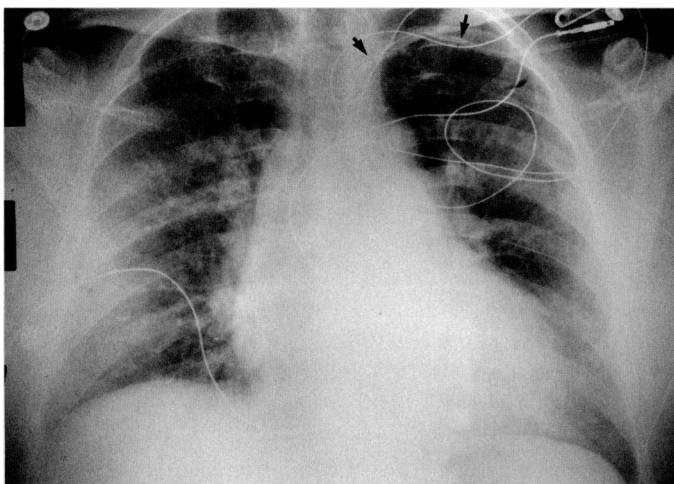
FIG. 1. A portable chest radiograph demonstrates cardiomegaly with a prominent left ventricular configuration. There is pulmonary vascular congestion and interstitial edema. A central venous catheter is noted *(arrows)*.

patient was desperately ill and had severely depressed ventricular function, I think this procedure was an appropriate therapeutic intervention. His limiting clinical problem was ventricular arrhythmias. In order to optimize arrhythmia therapy, a stable hemodynamic state is essential. Moreover, the issue of potentially more definitive therapeutic interventions such as aneurysectomy and coronary revascularization could be addressed only after diagnostic cardiac catheterization. Without IABP support, there would be an unreasonably high risk of complications during angiography.

At catheterization, the presence of a large ventricular aneurysm was confirmed. Coronary angiography demonstrated single-vessel coronary artery disease with a 90 percent residual stenosis in the proximal left anterior descending artery (LAD). The patient's attending physicians elected to pursue medical management, perhaps because they anticipated little benefit from surgical intervention in the absence of documented critical stenoses jeopardizing non-infarcted myocardium.

The patient was started on Amiodarone for control of ventricular tachycardia. The IABP was successfully weaned, and the patient remained stable enough to allow
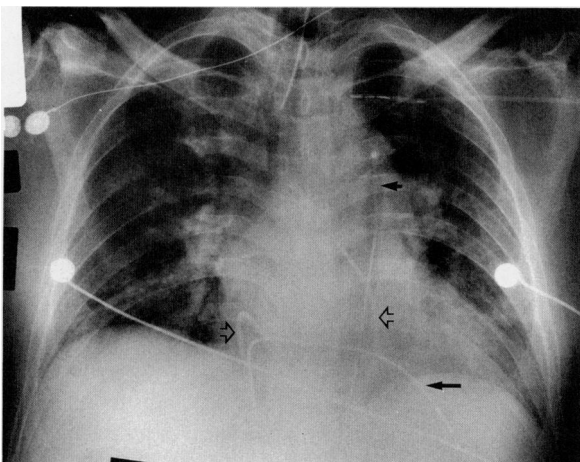

FIG. 2. A follow-up film obtained the next day shows persistent congestive heart failure. An endotracheal tube and intra-aortic balloon pump *(short arrow)* are in good position. A Swan-Ganz catheter *(open arrows)* and transvenous pacer *(long arrow)* have been inserted via a femoral approach.

transfer to the cardiac step-down unit. I should mention that our cardiac electrophysiology group has had remarkable success in bringing ventricular arrhythmias under control in patients with severely depressed cardiac function. Although Amiodarone has some direct myocardial depressant effects, the integrated effects of all of its pharmacologic properties in patients with poor left ventricular function usually result in no change in overall cardiac performance. Amiodarone can worsen heart block, although the protocol makes no note of such an occurrence in this presumably well-monitored patient.

After transfer to the step-down unit, the patient was apparently free of significant arrhythmias on monitoring. He did have anemia and required packed red cell transfusions. Anticoagulation therapy, which had been initiated for his deep venous thrombosis, was therefore discontinued. No mention is made of an anemia work-up.

On this new baseline of stable cardiac function, the patient collapsed six weeks following his index infarction and could not be resuscitated. We can now consider the differential diagnosis of late in-hospital death post-MI. Because the patient's demise was rapid, I will assume that there was a severe degree of acute mechanical or electrical cardiac dysfunction. In view of the patient's clinical course prior to death, I think the discussion of the differential diagnosis can be focused on the following: (1) ventricular fibrillation, (2) cardiogenic shock due to infarct extension, (3) cardiac tamponade, (4) vascular collapse from acute blood loss, and (5) massive pulmonary embolus.

Arrhythmias were a prominent feature in this patient's entire clinical course and certainly deserve primary consideration as the etiology of his sudden demise. In-hospital ventricular tachycardia and fibrillation occurring in monitored patients are usually successfully converted. This patient's ventricular irritability appears to have been well controlled on Amiodarone. For these reasons, I would consider the diagnosis of an arrhythmic event leading to death less likely than several other possibilities in the differential.

Recurrent infarction or infarct extension with rapid hemodynamic decompensation is unlikely on several grounds. First, the patient had only one significant lesion at catheterization, and the size of his infarct suggests that all myocardium supported by this coronary artery was irreversibly injured. Thus, recurrent ischemia with infarct extension seems unlikely. Second, although patients with infarct extension following a large MI may die of cardiogenic shock, the course tends to evolve over hours and not minutes.

Several factors in this case lead us to consider the possibility of acute cardiac tamponade. The protocol does not indicate whether the patient had a temporary pacemaker in place at the time of death. If present, it may have perforated the right ventricular wall, causing an acute hemopericardium with tamponade. Temporary transvenous pacemaker perforations of the right ventricle are rather common, though usually clinically silent. Apparently, adjacent pericardial tissue effectively contains the myocardial rent and prevents severe hemodynamic deterioration. Anti-coagulated patients are more likely to suffer rapid hemodynamic decompensation from perforation. Since this patient was not anti-coagulated, I will move on to other possibilities, although pacemaker perforation remains an important diagnostic consideration.

For reasons discussed earlier, cardiac tamponade precipitated by acute rupture of a ventricular free wall must be considered. Ruptures most typically occur between days three and five following acute myocardial infarction, rarely occur after three weeks,

and, in the absence of reinfarction or pseudoaneurysm formation, have not been reported beyond one month following infarction [4]. Based on this simple fact, I would not consider further the diagnosis of cardiac rupture.

Although cardiac rupture is unlikely, rupture of a pseudoaneurysm is an interesting consideration. A ventricular pseudoaneurysm represents a pericardial sac without myocardial elements formed by a contained cardiac rupture. Pseudoaneurysms expand over time and are said invariably to rupture. Characteristically, a pseudoaneurysm has a narrow neck connecting it to the true ventricular chamber. There are other angiographic features which usually help to distinguish pseudo from true ventricular aneurysms. I will assume that our angiographers would have astutely picked up this diagnosis at the time of cardiac catheterization.

Leaving primary cardiac events as a cause of death, I would first consider the category of vascular collapse due to occult and sudden loss of blood. IABPs occasionally cause life-threatening vascular trauma secondary to arterial perforation or dissection. Such problems are usually evident at the time of insertion or within the first 24 hours. This patient died several days following discontinuation of IABP therapy, and I will therefore discard this diagnosis. Acute gastrointestinal (GI) bleed is, of course, a consideration in any critically ill patient. Indeed, this patient had received blood transfusions to "maintain his hematocrit." Although occasionally catastrophic death follows an acute GI bleed in patients with severe ventricular dysfunction, the course is not typically abrupt and sudden as in this case.

Finally, we consider the possibility of pulmonary embolus, which not long ago was one of the major causes of morbidity and mortality following myocardial infarction. As already noted, this patient developed thromboembolic disease of his left lower extremity, possibly initiated by devices inserted through the femoral venous system and exacerbated by the long period of bed confinement. The patient received less than two weeks of therapy for the deep venous thrombosis (DVT) before anticoagulation was discontinued, clearly sub-optimal therapy. The significance of clinically apparent deep venous thromboses involving the large thigh veins is quite impressive. For instance, in post-operative patients, if DVT of femoral or popliteal veins is diagnosed but not treated, 40 percent of patients go on to have clinically apparent pulmonary emboli [5].

We are thus left with this one compelling diagnostic consideration: massive pulmonary embolus. Along with this patient's many cardiac-related problems, a relatively straightforward clinical problem developed in parallel: deep venous thrombosis. Anticoagulation was appropriately started but then terminated too early because of suspected bleeding problems. Upon ambulation, the patient probably dislodged a large thrombus from the deep thigh veins, leading to massive pulmonary embolus and death from acute right heart failure. I believe the patient died suddenly from this common but infrequently diagnosed cause of in-hospital death which sadly and unexpectedly interrupts the life of otherwise successfully managed patients.

Clinical Diagnosis

Massive pulmonary embolus

Pathologic Discussion

DR. STUART D. FLYNN *(Assistant Professor of Pathology):* As thoroughly discussed by Dr. Lee, the patient presented today finally appeared to be improving after a myocardial infarct and a complicated hospital course only to expire suddenly 45 days
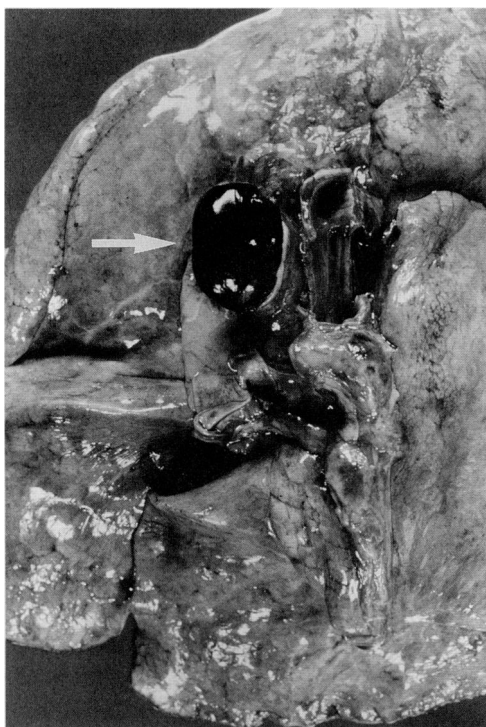
FIG. 3. An embolus *(arrow)* completely occludes the right main pulmonary artery.

later. The occurrence of a patient dying suddenly in the setting of apparent clinical improvement comprises a not insignificant percentage of autopsies performed at large medical centers. In this particular case, the probable cause of death seems limited and includes primary cardiac problems such as extension of his recent myocardial infarct or rupture of the left ventricle wall or a secondary manifestation such as massive pulmonary emboli.

Examination at autopsy was limited to the thorax only. The pleural cavities contained a relatively small amount (200 ml) of serous fluid, with 50 ml of sero-sanguineous fluid present in the pericardial sac. All of these serous surfaces were smooth and glistening, without evidence of an exudate. The heart was slightly enlarged, weighing 520 grams. Correlating with the clinical findings, there was pronounced atherosclerosis of all three major coronary arteries with the left anterior descending, left circumflex, and right coronary arteries exhibiting 90 percent, 65 percent, and 60 percent occlusion, respectively. Sectioning of the heart revealed marked thinning of the anterior and lateral walls of the left ventricle, indicative of an old infarct. Histologically, these areas were fibrotic with only a few residual myocytes identified. These are features of an infarct that occurred more than four weeks prior to death, again corresponding with this patient's history.

Of greatest relevance to this patient's sudden demise, both the left and right main pulmonary arteries were occluded by emboli (Fig. 3). In addition, several smaller branches of the pulmonary arterial vasculature contained emboli, and there was an associated recent right lower lobe infarct. Although the emboli probably originated in the deep veins of the legs, no thrombi were palpated and dissection of these vessels was not permitted.

Venous thromboemboli are a major cause of morbidity and mortality. It has been

estimated that some 50,000 people per year die in the United States from pulmonary emboli [6]. Since it is estimated that no more than one out of ten embolic events is fatal, more than 500,000 patients probably experience pulmonary emboli annually. Routine autopsy data reveal an incidence of pulmonary emboli of 20 to 30 percent, whereas studies in which special attention is directed toward the pulmonary vascular bed report an incidence as high as 60 percent [7].

The first description of massive occlusion of the pulmonary artery was reported by Tulpius in 1641 (as cited by Liebow [8]). It became apparent in the nineteenth century that the emboli were originating in the deep veins of the legs. Virchow emphasized the importance of slowing of the bloodstream as a factor predisposing to thrombus formation [9]. As it became clear in the 1930s and 1940s that the incidence of pulmonary emboli was increasing dramatically, attention began to be focused on how best to diagnose these thromboembolic events [10].

It has been estimated that 95 percent of all pulmonary emboli arise from thrombi in the deep venous system of the lower extremities and that five million patients per year in the United States develop an episode of deep venous thrombosis [6]. Autopsy studies have revealed that early microscopic thrombi were found in the pockets of valve cusps, in saccules in the vein wall, and at vein junctions [11]. Six primary sites have been described: *(1)* the iliac vein, especially the external iliac vein; *(2)* the common femoral vein; *(3)* the termination of the deep femoral vein, usually at a valve cusp at its ostium; *(4)* the popliteal vein, distal to the adductor ring and at a relatively large valve; *(5)* the posterior tibial veins; and (6) the intramuscular veins of the calf, especially the soleal veins. Although thrombi within veins of the calf muscles are most common, many significant pulmonary emboli arise from thrombi within the large deep veins of the legs, especially those above the knee [12]. Thrombosis at one site is independent of thrombosis elsewhere, and it is often a bilateral process.

Finally, there are several well-defined risk factors associated with the development of venous thromboembolism [13]; these include surgical trauma, immobilization, malignant disease, obesity, age (older than 40 years), myocardial infarct, and heart failure, the last three of which pertain to this patient. It has been estimated that fatal pulmonary emboli develop post-operatively in 0.1 percent to 0.8 percent of patients who undergo elective hip surgery, and 4 percent to 7 percent of patients who have emergency hip surgery [13]. Like this patient, the majority of patients who die of pulmonary emboli do so with little or no warning. Two-thirds of patients who die succumb within 30 minutes of the acute event, and, in many cases, the diagnosis is not established until after the patient's death.

Pathological Diagnosis

Sudden death secondary to massive pulmonary emboli; large left ventricle myocardial infarct

REFERENCES

1. Schuster EH, Bulkley BH: Expansion of transmural myocardial infarction: A pathophysiologic factor in cardiac rupture. Circulation 60:1532–1538, 1979
2. Meizlish JL, Berger HJ, Plankey M, et al: Functional left ventricular aneurysm formation after acute

anterior transmural myocardial infarction: Incidence, natural history, and prognostic implications. N Engl J Med 311:1001–1006, 1984

3. Phibbs B, Marriott HJL: Complications of permanent transvenous pacing. N Engl J Med 312: 1428–1431, 1985

4. Cohen M, Packer M, Gorlin R: Indications for left ventricular aneurysmectomy. Circulation 67:717–722, 1983

5. Kakkar VV, Howe CT, Flanc C, et al: Natural history of postoperative deep-vein thrombosis. Lancet ii:230–233, 1969

6. Moser K: Diagnostic approaches to pulmonary embolism. J Respir Dis 2:78–91, 1981

7. Freiman DG, Suyemoto J, Wesslers S: Frequency of pulmonary thromboembolism in man. N Engl J Med 272:1278–1280, 1965

8. Liebow AA: Cardiopulmonary disease. In Pathology of the Heart. Edited by SE Gould. Springfield, IL, Charles C Thomas Publishers, 1960, p 958

9. Virchow R: Gesammelte Abhandlungen Zur Wissenschaftlichen Medizin. Frankfort-am-Main, Von Meidinger Sohn, 1856

10. Belt TH: Thrombosis and pulmonary embolism. Am J Path 10:129–144, 1934

11. Sevitt S: Pathology and pathogenesis of deep vein thrombi. In Pulmonary Thromboembolism. Edited by KM Moser, M Stein. Chicago, Year Book Medical Publishers, 1973, p 93

12. Sevitt S, Gallagher NG: Venous thrombosis and pulmonary embolism. A clinicopathological study in injured and burned patients. Br J Surg 48:475–489, 1961

13. Raskob GE, Hull RD: Deep venous thrombosis: Can you prevent it? J Respir Dis 7:71–77, 1986